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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,815	03/29/2002	Preeti Lal	PF-0673 USN	2966

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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,815	LAL ET AL.	
	Examiner	Art Unit	
	Robert B Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *07 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-15 and 23-27* is/are pending in the application.

4a) Of the above claim(s) *1,2,9,12-15 and 23-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6, 8 and 10-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to amendment filed May 04, 2004. **Claims 7 and 16-22** are cancelled. **Claims 1-6, 8-15 and 23-27** are pending. **Claims 1-2, 9, 12-15, 23-27** are withdrawn. **Claims 3-6, 8 and 10-11** are currently under examination.

Withdrawal of Objections and Rejections

The rejection of **claim 3-6, 8 and 10-11** under 35 U.S.C § 112, second paragraph is withdrawn.

Maintenance of rejections

Claim Rejection - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-6, 10 and 11 are rejected under U.S.C 101 because the claimed invention is not supported by either specific and substantial asserted utility or well established utility.

Claims 3-6, 10 and 11 are directed to isolated nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO: 10 that encode the protein comprising the amino acid sequence of SEQ ID NO: 5. The instant specification discloses that the polypeptides comprising the amino acid sequence presented in SEQ ID NO: 5 is a protein that shares structural and sequence similarity with leukocyte and blood associated proteins (LBAP).

Pages 27-52 of the instant application describes the uses and methods of the invention, and state that the nucleic acid molecules and proteins can be used in methods such as screening, detecting assays (labeled hybridization, PCR probes for detecting sequences and predicative medicine), production of expression vectors, manufacture of medicament for the treatment of a variety of diseases, production of anti-bodies for diagnostic purposes. The specification also states that the leukocyte and blood associated proteins of the invention have structural similarity with putative haemopoietic membrane proteins. The specification further asserts that the leukocyte and blood associated proteins and leukocyte and blood associated nucleotide sequences, can be used for screening for drugs (or high throughput screening of cDNA libraries) effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of the immune system of the body and can be used directly to treat disease and disorders.

However these are not considered to be specific or substantial utilities for either the nucleic acid molecules or proteins. The methods such as recombinant production of protein, southern blotting, PCR, detection assays, antibody production, complementary sequence hybridization, EST production, microarray production and DNA probe production are considered to be general methods, and are not considered to be specific and substantial utilities.

It is asserted in the specification that the leukocyte and blood associated protein (LBAP) encoded by leukocyte and blood associated polynucleotide has structural similarity with putative haemopoietic membrane proteins. Kaline et al and Baird et al.

(cited in IDS filed November 12, 2003) disclose polynucleotides that encode polypeptides that are putative haemopoietic membrane proteins. However, the polypeptide of the invention encoded by the isolated polynucleotide sequence disclosed, has not been shown to have primary structural similarity with polypeptides encoded by polynucleotides present in Baird et al. and Kanline et al. . Also, there is no disease or disorder correlated with the leukocyte and blood associated protein (LBAP) encoded by the nucleic acid sequence of the invention. The use of unknown amino acids encoded by polynucleotides, to determine structural similarity with other amino acid sequences by itself does not constitute a specific and substantial utility. Based on structural similarity alone, the specification attempts to assert that the new cDNA clone encodes a putative haemopoietic membrane protein. However function prediction from structure or structure prediction from function is not a reliable measure of utility. leukocyte and blood associated protein (LBAP) encoded by novel leukocyte and blood associated polynucleotide does not appear to have structural similarity to haemopoitic membrane proteins, but even if they did demonstrate a level of structural homology, since the function of leukocyte and blood associated protein (LBAP) is not known it would not be conclusive to assume, solely based on structure homology, that they have the same function and would have the same utility. It is necessary to carry out further characterization of this protein to asses the patentable utility, of the polynucleotide.

The specification discloses that the leukocyte and blood associated nucleic acid can be used for hybridization probes for screening libraries and microarray-based

analysis. However these are not considered to be specific and substantial utilities. The utilities described are general and would apply to any polynucleotide.

In Brenner v. Manson, 148 U.SP.Q 689 (Sup. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to posses anticancer activity was alleged to be useful because the compound produced thereby was potentially useful as anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polynucleotides encoding novel human proteins which have undetermined function or biological significance. Thus no actual or specific activity is attributed to the proteins identified in the specification as novel human proteins or the polynucleotides encoding them.

In **claims 5-6** the claimed transformed cell with a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide sequence disclosed by SEQ ID NO: 10, is not supported by well established utility: cells may be used for expressing nucleic acid sequences but this is not a specific utility, because the use of the cell is generally applicable to any expression vector, and therefore the utility is not particular to the sequence being claimed for the cell. Moreover, the sequence itself does not provide for specific utility, as the function of sequence disclosed has not

been determined in any art of record or shown in the application. Therefore, no specific utility is found for the claimed subject matter.

With regard to substantial utility, the claimed cell line is not supported by a substantial utility because the specification states that the cells can be used to express polypeptides of interest (page 49, example IX). A starting material that can only be used to produce a final product does not have a substantial utility. In this case the DNA sequence used to produce the protein of interest does not have an asserted or identified substantial utility. The proposed research strategies to characterize potential products, specifically in regards to biological activities, do not constitute a substantial utility or a "real world use".

Because the claimed invention is not supported by a specific and substantial asserted utility for the reasons above, credibility has not been asserted. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the protein such that another non-asserted utility would be well established for the cell line.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3-6, 10 and 11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and

substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if the specification were enabling of how to use the leukocyte and blood associated nucleic acid molecules and proteins, enablement would not be found to be commensurate in scope with the claims. As discussed in ***USC 101 and 112*** rejections above, the specification has not taught the skilled artisan how to use the nucleic acid molecule and polypeptide of SEQ ID NO: 10 and 5 that are disclosed in the instant specification. If one skilled in the art does not know how to use these nucleic acid molecules, the skilled artisan would clearly not know how to use the nucleic acid molecules encoding polypeptides that have structural similarity with haemopoietic membrane bound proteins.

Claims 3-6, 10 and 11 are rejected under 35 U.S.C 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The claims as presented encompass genomic DNA. The leukocyte and blood associated Protein clone was obtained from a cDNA library. The structure and sequence of the chromosomal DNA is not disclosed in the sufficient detail, so that one skilled in the art can reasonably conclude that the inventors had possession of the claimed invention. The person skilled in the art would not recognize in the current disclosure a description of the invention defined by the claim as it relates to genomic DNA for several reasons. Genes are extremely complex structures made of exons (presented in cDNAs corresponding to the

genomic DNA) and introns (non-coding regions between the exons). The prior art does not teach genomic DNA corresponding to the disclosed cDNA or a family of proteins to which the current claimed encoded protein belongs for which there is a known conservation of encoding genomic structure. There are no general rules for predicting the number of exons and introns the genomic DNA would expect to have. The prediction is even more complicated due to the possibility of splice variants, so that the disclosed cDNA may not disclose all exons within the corresponding DNA because the alternative exons are particular to individual splice variants. Even acknowledging high skill in molecular biology art, prediction of even the general structure of the claimed polynucleotide (*i.e.* number and general size of exons and introns), let alone the sequence of the polynucleotide, is not possible based on the information provided in the specification. There are no examples of genomic DNA disclosed. The coding sequences disclosed do not contain any introns sequence(s) since the sequences are cDNA, which is made of only exon sequences. It is not apparent that the claimed polynucleotide encompassing genomic DNA was obtained when the application was filed, nor was there any written description of such. For these reasons, it does not appear that applicants were in possession of the claimed invention as it pertains to genomic DNA at the time the application was filed. Because the specification merely discloses cDNA sequences, and does not describe the corresponding genomic DNAs, the written description requirement has not been met with respect to genomic DNA.

Response to applicant's arguments

The Applicants assert that the nucleic acid of the invention has utility because it can be used in a microarray assay or it can be used as a nucleic acid probe. The Applicants further assert that the polypeptide encoded by the nucleic acid of the invention has 77% homology with a mouse haemopoietic membrane protein, JB542 (g3355655).

The Examiner would like to state that all the above points were addressed in the original rejection. General uses, such as a microarray assay, that apply to any nucleic acid molecules are considered to be specific that the particular nucleic acid and are not given patentable weight. Also, the determination of function from structure is not a sufficient means of determining the specific utility of a polypeptide. Again all these points were explained at great length in the initial utility rejection.

Applicants have provided declarations of Rockett, Iyer, and Bedilion and a host of references to support their view (which have not been provided on a PTO 1449).

Dr. Rockett discusses the importance of using polynucleotide and polypeptides expression profiling using a model of expression profile or a pattern of genes and protein expressed by treatment with known testicular toxins as standards, signatures, or fingerprints. Dr. Rockett's expertise and points are appreciated and well-taken. However, the specification does not establish any toxin which would induce the expression of SEQ ID NO: 5 expression so that SEQ ID NO: 5 can be a part of a pattern of expression in response to the toxin. Without this demonstration, the utility as

a part of a pattern of gene expression induced by a toxin or like toxin is lost. It is not enough to say that SEQ ID NO: 5 can be used in expression profiling; rather, in which toxin specific expression profile is SEQ ID NO: 5 expressed?

Dr. Iyer discusses drug target validation and identity of secondary drug effects using expression profiling. Dr. Iyer's comments are well-taken. However, the specification does not establish any drug or pharmaceutical which would induce the expression of SEQ ID NO: 5 expression so that SEQ ID NO: 5 can be a part of a pattern of expression in response to the drug. Without this demonstration, the utility as a part of a pattern of gene expression induced by a drug is lost. It is not enough to say that SEQ ID NO: 5 can be used in expression profiling; rather, in which drug specific expression profile is SEQ ID NO: 5 expressed?

Dr Bedilion discusses the commercial need of customers to have more and more genes on each array. The customers use the array as a research tool, that is, they expose the array comprising many polynucleotides or polypeptides to toxins or drugs and detect the resulting expression pattern. However, the specification does not establish any toxin or drug which would induce the expression of SEQ ID NO: 5 expression so that SEQ ID NO: 5 can be a part of a pattern of expression in response to the toxin or drug. Without this demonstration, the utility as a part of a pattern of gene expression induced by a toxin or like toxin is lost. It is not enough to say that SEQ ID NO: 5 can be used in expression profiling; rather, in which toxin or drug specific expression profile is SEQ ID NO: 5 or NO: 22 expressed?

At page 9, Applicants discuss the legal standard for 35 USC 101 and 112. While Applicants do not specifically argue the rejection, it appears that their point is that if a person of ordinary skill in the art would understand how to use the invention then it has utility. Again, in which toxin or drug specific expression profile is SEQ ID NO: 5 expressed?

At pages 10-25, Applicants urge that SEQ ID NO: 5 can be used in disease detection and diagnosis, and in toxicology testing. More information must be provided to establish this utility. For example, which disease is the expression of SEQ ID NO: 5 associated with? How will it be used to detect or diagnose the disease? In response to which toxin with they be expressed?

Furthermore the Applicants assert that the Guidelines are themselves inconsistent with the law at pages 11-21. The Examiner will only address parts of this critique as it applies to the instant invention and rejection.

Applicants assert that the use of expression profiling has a well-established utility as tools for toxicology testing, drug discovery, and diagnosis of disease (IA at page 11-13). As noted above, what toxicology testing that the expression pattern will aid in determining, what drug will be developed by knowing this expression pattern, or what disease will be diagnosed by knowing this expression pattern is not provided. Applicants are asking others to use their polypeptide to determine what it is useful for - the toxicology of nicotine? the development of drugs to treat Alzheimer's? the diagnosis of breast cancer? for example. Therefore, this argument is not persuasive.

Applicants assert that the use of LABP-5 proteins for toxicology testing, drug discovery, and diagnosis of disease because practical, beneficial use and not functionality is at the core of the utility requirement (IIA at page 13-16). Applicants assert that the claimed inventions is known to be useful, for example, in toxicology test to determine whether a drug or toxin changes the expression pattern of the protein, or to determine whether a specific medical condition affects the expression of the protein, or serve as a marker for or to assess the stage of a particular disease or condition. Applicants do not provide any information regarding what drug or toxin will affect the expression pattern of the protein or what it may mean. Applicants do not provide any information as to any medical condition that may affect the expression pattern of the protein or what it may mean. Applicants do not provide any information as to what disease or condition the protein could be a marker for. As noted above, what toxicology testing that the expression pattern will aid in determining, what drug will be developed by knowing this expression pattern, or what disease will be diagnosed by knowing this expression pattern is not provided. Applicants are asking others to use their polypeptide to determine what the polypeptide is useful for - the toxicology of nicotine? the development of drugs to treat Alzheimer's? the diagnosis of breast cancer? for example. Therefore, this argument is not persuasive.

Applicants assert (IIB at pages 13-27) that the invention is a member of a broad class of DNA in general which include those sequences having utility. Therefore Applicants conclude that the generally utility for the class is sufficient for the claimed species and that all isolated and purified polynucleotide and polypeptide sequences

which are expressable can be and are used in a real-world context as tools for toxicology testing such as for drug discovery purposes. This argument is not persuasive for all of the reasons provided above.

Applicants argue (IC at pages 27-28) that the use of the protein as a research tool is a substantial utility and cite such uses as diagnosis of disease for example. Again, no disease is stated that can be diagnosed by knowing the expression pattern of the LABP-5 protein. Therefore, this argument is not persuasive because one skilled in the art would have to determine for themselves which disease could be diagnosed by knowing the expression pattern of the claimed protein.

Applicants assert (IID at page 28) that the sale of the sequences of the claimed polypeptide to databases is evidence of utility. This argument is noted but this deals with nonfunctional descriptive material, that is, the sequences of bases having no known function. While the arguments deal with the database, the database structure may or may not be patentable, the data in the database is not patentable. Since the data is nonfunctional and descriptive material, the arguments are moot and not on point.

Applicants assert (IIB at pages 18-27) that the invention is a member of a broad class of DNA in general which include those sequences having utility. Therefore Applicants conclude that the generally utility for the class is sufficient for the claimed species and that all isolated and purified polynucleotide and polypeptide sequences which are expressible can be and are used in a real-world context as tools for toxicology testing such as for drug discovery purposes. This argument is not persuasive for all of the reasons provided above.

Applicants argue (IC at pages 27-28) that the use of the protein as a research tool is a substantial utility and cite such uses as diagnosis of disease for example. Again, no disease is stated that can be diagnosed by knowing the expression pattern of the LABP-5 protein. Therefore, this argument is not persuasive because one skilled in the art would have to determine for themselves which disease could be diagnosed by knowing the expression pattern of the claimed protein.

Applicants assert (IID at page 29) that the sale of the sequences of the claimed polypeptide to databases is evidence of utility. This argument is noted but this deals with nonfunctional descriptive material, that is, the sequences of bases having no known function. While the arguments deal with the database, the database structure may or may not be patentable, the data in the database is not patentable. Since the data is nonfunctional and descriptive material, the arguments are moot and not on point.

In view of the restriction requirement, the examiner would like to point out that presently unity of invention does not exist since the product is not considered to be allowable subject matter.

Conclusion

No claims are allowed

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBMor

Robert B. Mondesi
Patent Examiner
Group 1653
07/06/04

ROBERT A. WAX
PRIMARY EXAMINER